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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/542,445	04/04/00	STAPLES M	BEH-7354A-DI

HM12/0904

LOIS K RUSZALA
C/O DADE BEHRING INC
1717 DEERFIELD RD #778
DEERFIELD IL 60015-0778

EXAMINER	
DEVI,S	
ART UNIT	PAPER NUMBER
1645	9

DATE MAILED: 09/04/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/542,445	Staples et al.
Examiner	**Art Unit**
S. Devi, Ph.D.	1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jun 7, 2001* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-3* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-3* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☒ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *8* ,
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

Applicants' Preliminary Amendment

1) Acknowledgment is made of Applicants' preliminary amendment filed 06/07/01 (paper no. 7) in response to the restriction requirement mailed 04/24/01 (paper no. 4).

Status of Claims

2) Claims 4-39 have been canceled via the amendment filed 06/07/01.

Claims 1-3 are pending and are under examination.

Change of Address & Docket Number

3) Acknowledgment is made of Applicants' notification of the change of address filed 06/11/901 (paper no. 5).

Information Disclosure Statement

4) Acknowledgment is made of Applicants' Information Disclosure Statement filed 06/03/00 (paper no. 8). The information referred to therein has been considered and a signed copy is attached to this Office Action (paper no. 9).

Abstract

5) The abstract of the disclosure is objected to because the abstract, as amended, the number of words contained in the abstract exceeds the number of words permitted. Correction is required. See MPEP § 608.01(b).

Priority

6) The instant application is a Divisional of application SN 08/896,244 filed 07/17/97, now US patent 6,171,801, which claimed priority to the provisional application, SN 60/022,133, filed 07/18/1996.

It is noted that, in the instant case, priority to the provisional application has not been claimed either in the oath or first paragraph of the specification.

Specification - Informalities

7) The specification is objected for the following reasons:

(a) The first paragraph of the specification requires amendment if Applicants wished to claim priority to the provisional application. See above under the item 'Priority'.

(b) The use of the trademark in the instant specification has been noted. For example, see page 27: "Pluronic 25R2 (see page 27). The recitation should be capitalized wherever it appears and be accompanied by the generic terminology. Each letter of the trademark must be capitalized. See M.P.E.P 608.01(V) and Appendix l. Although the use of trademarks is permissible in patent applications, the propriety nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks. It is suggested that Applicants examine the whole specification to make similar correction to the trademark, wherever it appears.

Double Patenting Rejection

8) The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970) and *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 C.F.R 1.321(c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 C.F.R 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 C.F.R 3.73(b).

(a) Claims 1-3 are rejected under the judicially created doctrine of obviousness-type double patenting over claims 1-4 of the patent, US 6,171,801. Although the conflicting claims are not identical, they are not patentably distinct from each other, because of their overlapping scope.

(b) Claims 1-3 are rejected under the judicially created doctrine of obviousness-type double patenting over claims 1, 2, 4, 5, 10, 11, 26 and 27 of the patent, US 6,159,698. Although

the conflicting claims are not identical, they are not patentably distinct from each other, because of the overlapping scope.

Rejection(s) under 35 U.S.C § 102

9) The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> **(e)** The invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

10) Claims 1-3 are rejected under 35 U.S.C § 102(e) as being anticipated by Khanna *et al.* (US 4,798,804).

Khanna *et al.* teach a method for releasing a ligand from a complex comprising contacting a sample (i.e., medium) suspected of containing the complex with an effective amount of a releasing agent. A preferred releasing agent is a methoxybenzoic acid (see the abstract and column 3, lines 35-57). The sample containing the ligand is usually a body fluid such as blood serum, blood plasma or whole blood (see column 2, lines 1-4).

Claims 1-3 are anticipated over Khanna *et al.*

Relevant Prior Art

11) The prior art made of record and not relied upon is considered pertinent to Applicants' disclosure.

- Kaufman *et al.* (CA 2,014,233 - Applicants' IDS) teach the use of benzoic acid as a releasing agent to release a drug ligand from a complex (see page 5). The contacting of the sample with the releasing agent is performed in a single step.
- Strinna Erre *et al.* (*Polyhedron* 6(10): 1869-1874, 1987) teach the decomposition of methoxybenzoate complexes and a mechanism which involves the shift of a CH_3 group from a ligand molecule to the carboxylic group of a second ligand, to give the methyl ester of the parent methoxy- or dimethoxy-benzoic acid. It is taught that the decomposition step appears to be dependent on the ring substitutions of the ligands, and that a methoxyl group in an *ortho*-position to the carboxylate function activates the decomposition process (see the abstract and page 1871).

Basak (*Asian J. Chem* 5(2): 316-318, 1993) teaches 2-, 3- and 4-methoxybenzoic acids as biologically active ligands. It is taught that methoxy group is an electron donating group.

- Pethe *et al.* (*Indian J. Chem* 15A: 998-1001, 1977) teach protonated ligands, methoxybenzoic acid and its various derivatives, and factors promoting dissociation of ligands.
- Shaw *et al.* (*Therapeutic Drug Monitoring* 17: 685-689, 1995) teach that mycophenolic acid is avidly bound to plasma proteins and human serum albumin. Substances that decrease the binding of mycophenolic acid to human serum albumin are taught.
- Langman *et al.* (*Therapeutic Drug Monitoring* 16: 602-607, 1994 - Applicants' IDS) teach the blood distribution of mycophenolic acid. It is taught that a substantial amount of mycophenolic acid is bound to plasma proteins other than lipoproteins and albumin.
- Carbelli *et al.* (US 4,332,786) and Allen (US 4,451,571) teach the conventional use of releasing agents to release ligands/analytes from interfering substances such as binding proteins before determining analyte levels.
- Lucanska *et al.* (*Zb. Celostatnej Konf. Term. Anal. 8th*: 255-258, 1979: Abstract) teach the decomposition of complexes with methoxybenzoate.
- Neumann *et al.* (US 4,559,291) teach the use of *o*-methoxybenzoic acid as a ligand releasing agent.
- Nowak *et al.* (*Clin. Chem.* 41/7: 1011-1017, July 1995 - Applicants' IDS) teach a method for releasing mycophenolic acid present in a medium of human plasma containing endogenous serum albumin by combining the medium with an amount of the releasing agent effective in releasing MPA from the complex (see Table 3). Nowak *et al.* teach that MPA falls into anionic or acidic class of drugs and binds to HSA (i.e. an endogenous protein) in the human blood (see page 1016). It is taught that "MPA is avidly and extensively bound to human serum albumin" and that certain drugs or chemicals (i.e. releasing agents) including salicylate can be used to displace or release MPA from its human serum albumin-binding sites by competitive displacement mechanism (see page 1016).
- Nishijo *et al.* (*Chem. Pharm. Bull.* 33: 2648-2653, 1985) teach a method of releasing a ligand from a complex formed with an endogenous protein such as serum albumin by

using benzoic acid. Benzoic acid is taught to release the ligand by competitive interaction with serum albumin (see abstract).

- Shaw *et al.* (*Therapeutic Drug Monitoring* 17: 685-689, 1995) teach that mycophenolic acid is avidly bound to plasma proteins and human serum albumin, i.e. endogenous proteins. Substances that decrease the binding of mycophenolic acid to human serum albumin are taught.

- Bowmer *et al.* (*J. Pharm. Pharmacol.* 37: 812-815, 1985) teach the ability of benzoic acid to bind to human albumin by competitive displacement mechanism.

Remarks

12) Claims 1-3 stand rejected.

13) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center located in Crystal Mall 1. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The CM1 facsimile center's telephone number is (703) 308-4242, which is able to receive transmissions 24 hours a day and 7 days a week.

14) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (703) 308-9347. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

S. Devi, Ph.D.
Primary Examiner
August 2001